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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,789	05/15/2001	Pablo Rubinstein	63475/267	9553

7590 07/26/2005

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EXAMINER	
BIANCO, PATRICIA	
ART UNIT	**PAPER NUMBER**
3761	

DATE MAILED: 07/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/855,789	RUBINSTEIN ET AL.	
	Examiner	Art Unit	
	Patricia M. Bianco	3761	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,27-32,34-38,41-47,52,53 and 74-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,27-32,34-38,41-47,52,53 and 74-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

In the amendment filed 05/06/2005, Claims 33, 48, 49, & 54-73 have been cancelled, claims 74-77 have been added and claims 25, 34, 36, & 41 have been amended. As a result, claims 25, 27-32, 34-38, 41-47, 52, 53, & 74-77 are currently pending.

Response to Arguments

Applicant's arguments filed 5/6/05 have been fully considered but they are not persuasive with respect to claims 25, 27-32, 34-38. Also, with respect to claims 41-49 & 52-53, new ground(s) of rejection are presented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 41-53, 74, 75, & 77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide reasonable disclosure, such as evidence or data, that shows that

applicant was in possession of the invention as now claimed at the time of filing. The scope of the claim is outside the detailed description. The specification does not provide an adequate written description such that the claimed product is obtained such that *when thawed* the white blood cells have a viability greater than 90% with respect to cord or placental blood any person skilled in the art to make and use the subject matter defined without undue experimentation. It is unclear as to how such a viability is achieved. The specification does not set forth the best mode contemplated by the inventor of carrying out his or her invention.

Claim Rejections - 35 USC § 102/35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 25, 27, 30-32, 34-36, 38-47, 52, 53, & 74-77 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Boyse et al. (5,004,681).

It is the position of the examiner that the "therapeutic product" claimed is mostly separated white blood cells and a cyroprotective agent that has a cell viability greater than 80% (as required by independent claims 25 & 41 and their dependent claims) or viability greater than 90% (claim 34, and claim 41 & its dependents). Boyse et al. discloses cryopreservation of hematopoietic stem and progenitor cells (i.e. white blood cells) of blood therefore anticipates or, in the alternative, renders obvious the claimed invention. Boyse et al. discloses that the cells have a cyroprotective agent in a low concentration to result in viable cell counts of greater than 80% and 90% (see Table III for Viability percentages & col. 22, line 25-col. 24, line 10). The cells may be obtained from cord blood and/or placental blood (col. 12, lines 54-60). The blood had an anticoagulant, such as CPD or ACD, added to it and therefore the cells will inherently have residual anticoagulant in the product. The cells also will have a cyroprotective agent added to them, such as DMSO or dextran. With respect to the use of DMSO and its concentration, Boyse et al. states that to circumvent cell injury cryoprotectant agents are used in low concentrations that are nontoxic to cells and control of the freezing rate is maintained. Boyse teaches that a low concentration of DMSO is used (col. 12, lines 25-68). Boyse also teaches that dilution of the cyroprotective agent to an insignificant concentration will reduce the adverse affects of recovered, thawed cells (col. 24, lines 50-68). Applicant also claims that the white cell viability is tested using DNA fluorescence stain (claims 39 & 52) and that the red to white cell count is approximately 100 to one (claims 76 & 77). These limitations are seen as a recitation of the intended use for calculating the product viability and it has been held that a recitation with respect

to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed product from a prior art apparatus satisfying the claimed structural limitations. *Ex parte Masham*, 2 USPQ2d 1647 (1987). Boyse also teaches that erythrocytes may be removed from the whole blood collected by well known physical and/or immunological cell separation procedures, leaving white blood cells. Since applicant requires less than 10% of red blood cells, this limitation is met since none to few red blood cells will be left.

In the alternative, the claims are seen to be rejected as being obvious over Boyse et al.. With respect to the cell viability being greater than 80% or greater than 90%, it would be obvious to modify the concentration of cyroprotective agent added to the cells to achieve greater than 80% or 90% viability, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. With respect to the claimed limitations specific to the concentrations of DMSO used (10% DMSO and 1% DMSO), the osmolarity of the product not more than 300 milliosmols and to the limitations requiring the volume of the product being contained in a volume of 3 mm to 20mm, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use a concentration of DMSO to be either 1% or 10%, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. Therefore, since Boyse et al. discloses that a low concentration of DMSO is used such general conditions are met.

With respect to the osmolarity of the product is not more than 300 milliosmols, it would have been obvious to one having ordinary skill in the art at the time the invention was made to achieve this osmolarity, since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28, 29, 43, & 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyse et al. ('681) in view of Livesey et al. (5,622,867). Boyse et al.

discloses the invention substantially as claimed, see rejection supra. Boyse et al., however, fails to disclose specifically of using a cyroprotective agent of DMSO being diluted to 50% with dextran. Boyse et al does teach that the cryoprotectant agent used may be chosen from DMSO or dextran.

Livesey et al. teaches of cryopreserved cells that have cyroprotective agent added to them to preserve cell viability. The cyroprotective agent may be DMSO, or dextran, individually or in combination. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use a concentration of DMSO to be diluted DMSO to 50% with dextran, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Response to Arguments

Applicant's arguments filed 05/06/2005 have been fully considered but they are not persuasive. With respect to independent claim 25, applicant argues that Boyse does not anticipate the claim because the product must have less than 10% of red blood cells. The examiner respectfully disagrees. Boyse teaches of separating the whole blood and storing the white blood cells. This separation inherently results in the removal of red blood cells. Since Boyse teaches of the removal of erythrocytes by standard techniques that result in the removal of a majority of erythrocytes, this limitation is met since none to few red blood cells will be left.

With respect to amended claim 41, applicant argues that Boyse does not teach of a resulting product that, when thawed, the white blood cells have a viability greater than 90% with respect to cord or placental blood. The examiner respectfully disagrees. Boyse teaches that an objective of the invention is to result in therapeutic cells that, upon thawing, have a high viability. Boyse further teaches of using a cryopreserving agent at a level that is very low to circumvent cell injury cryoprotectant agents and control of the freezing rate is maintained to achieve this. Boyse also teaches that dilution of the cyroprotective agent to an insignificant concentration will reduce the adverse affects of recovered, thawed cells (col. 24, lines 50-68). These practices will result in a high viability, as shown in table III.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia M. Bianco whose telephone number is (571) 272-4940. The examiner can normally be reached on Monday to Friday 9:00-6:30, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tanya Zalukaeva can be reached on (571) 272-1115. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

July 20th, 2005

PATRICIA BIANCO
PRIMARY EXAMINER

Patricia M Bianco
Primary Examiner
Art Unit 3761